8-30-00

ARC-14231-2

PATENT

Express Mail Label No.: EK380732495US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Box Patent Application
Commissioner for Patents
Washington, D.C. 20231

NEW APPLICATION TRANSMITTAL

Transmitted herewith for filing is the patent application of

Inventor(s): Robert W. Mah

For: Body Sensing System

1. Type of Application

This new application is for a(n)

- ☐ Original (nonprovisional)
- ☐ Design
- ☐ Plant
- ☐ Divisional.
- ☐ Continuation.
- ☒ Continuation-in-part (C-I-P).

2. Benefit of Prior U.S. Application(s) [35 U.S.C. 119(e), 120, or 121]

☒ The new application being transmitted claims the benefit of prior U.S. application(s). Enclosed are added pages (pages 5-7) for new application transmittal where benefit of prior U.S. Application(s) claimed.

3. Papers Enclosed

A. Required for filing date under 37 CFR § 1.53(b) (Regular) or 37 CFR § 1.153 (Design) Application

☒ specification (20 pages)

☒ claims (5 pages)

☒ drawings (6 sheets, including figs. 1-3, 4A-D, 5-7, and 8A-B)

☐ formal

☒ informal

☐ The enclosed drawing(s) are photograph(s), and there is also attached a "Petition to Accept Photograph(s) As Drawings." 37 CFR 1.84(b).

B. Other Papers Enclosed

☒ Declaration and Power of Attorney

☐ executed by inventor(s)

☐ legal representative of inventor(s)

☐ joint inventor or person showing a proprietary interest on behalf of inventor who refused to sign or cannot be reached

☐ This is the petition required by 37 CFR 1.47 and the statement required by 37 CFR 1.47 is also attached. See item 13 below for fee.

☒ Abstract (1 page)

☒ Express Mail Certificate (1 page)

☒ Return Postcard

4. Additional papers enclosed

☐ Preliminary Amendment

☐ Information Disclosure Statement (37 CFR 1.98)

☐ Form PTO-1449 (PTO/SB/08A and 08B)

☐ Citations

☐ Declaration of Biological Deposit

☐ Submission of "Sequence Listing," computer readable copy and/or amendment pertaining thereto for biotechnology invention containing nucleotide and/or amino acid sequence.

☐ Authorization of Attorney(s) to Accept and Follow Instructions from Representative

☐ Special Comments

☐ Other

5. Assignment

☐ An assignment of the invention to

☐ is attached. A separate

☐ "Cover Sheet for Assignment (Document) Accompanying New Patent Application" is attached.

☒ will follow.

6. Certified Copy

Certified copy(ies) of application(s)

Country	Application No.	Filed
Country	Application No.	Filed

from which priority is claimed

☐ is (are) attached

☐ will follow.

7. Fee Calculation (37 CFR 1.16)

A. ☒ Regular application

	CLAIMS AS FILED				
	Number Filed	Number Extra		Rate	Basic Fee $690.00
Total Claims	16	- 20 = -0-	x	$ 18.00	-0-
Independent Claims	2	- 3 = -0-	x	$ 78.00	-0-
Multiple dependent claim(s), if any			+	$260.00	-0-

☐ Amendment canceling extra claims is enclosed.

☐ Amendment deleting multiple-dependencies is enclosed.

☐ Fee for extra claims is not being paid at this time.

Filing Fee Calculation $690.00

8. Payment of Fees and Authorization to Charge Additional Fees or Credit Overpayment

☐ No filing fee is to be paid at this time.

☐ Check in the amount of _____ is enclosed.

☒ Please charge Deposit Account No. 14-0116 in the amount of $690.00. A duplicate of this transmittal is attached.

☒ The Commissioner is hereby authorized to charge an additional fee which may be required to effect the filing of this application or credit any overpayment to Deposit Account No. 14-0116.

☐ been filed on _____, in prior application no. , which was filed on .

☐ is (are) attached.

11. Maintenance of Copendency of Prior Application

A. ☐ Extension of time in prior application

☐ A petition, fee, and response extends the term in the pending prior application until .

☐ A copy of the petition filed in prior application is attached.

B. ☐ Conditional Petition for Extension of Time in Prior Application

☐ A conditional petition for extension of time is being filed in the pending prior application.

☐ A copy of the conditional petition filed in the prior application is attached.

12. Further Inventorship Statement Where Benefit of Prior Application(s) Claimed

(a) ☐ This application discloses and claims only subject matter disclosed in the prior application whose particulars are set out above and the inventor(s) in this application are

☐ the same.

☐ less than those named in the prior application. It is requested that the following inventor(s) identified for the prior application be deleted:

(b) ☒ This application discloses and claims additional disclosure by amendment and a new declaration or oath is being filed. With respect to the prior application, the inventor(s) in this application are

☐ the same.

☐ the following additional inventor(s) have been added:

(c) The inventorship for all the claims in this application is

☐ the same.

☐ not the same. An explanation, including the ownership of the various claims at the time the last claimed invention was made

☐ is submitted.

☐ will be submitted.

13. Abandonment of Prior Application

☐ Please abandon the prior application at a time while the prior application is pending, or when the petition for extension of time or to revive in that application is granted, and when this application is granted a filing date, so as to make this application copending with said prior application.

14. Petition for Suspension of Prosecution for the Time Necessary to File an Amendment

☐ There is provided herewith a Petition to Suspend Prosecution for the Time Necessary to File an Amendment (New Application Filed Concurrently)

15. Notification in Parent Application of This Filing

☒ A notification of the filing of this

☐ continuation

☒ continuation-in-part

☐ divisional

is being filed in the parent application, from which this application claims priority under 35 U.S.C. § 120.

Robert M. Padilla 8-28-00

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ARC-14231-2 PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re new application of: Robert W. Mah

Filed: Herewith

For: "Body Sensing System"

Box Patent Application
Commissioner for Patents
Washington, DC 20231

EXPRESS MAIL CERTIFICATE

"Express Mail" label number: EK380732495US

Date of Deposit: August 28, 2000

I here by certify that the attached correspondence comprising:

One Return Post Card
Certificate of Mailing (1 page)
Transmittal Letter (7 pages, in duplicate)
Specification & Claims (26 pages, including abstract)
Informal Drawings (6 sheets, including figs. 1-3, 4A-D, 5-7, and 8A-B)
Declaration/Power of Attorney (2 pages)

is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box Patent Application, Commissioner for Patents, Washington, DC 20231.

Vickie L. Kent
name of person depositing in mail

Vickie L. Kent 08/28/00
signature date

BODY SENSING SYSTEM

Origin of the Invention

The invention disclosed herein was made by employees of the United States Government and may be manufactured and used by or for the Government for governmental purposes without payment of any royalties for such manufacture and use. This application is a Continuation In Part of an application, U.S. Serial No. 09/017,519, filed 2 February 1998.

Field of the Invention

This invention relates to navigation to, and imaging, sensing, diagnosing, and providing a prognosis for a medical condition of, a target site within a human or animal body.

Background of the Invention

Use of a conventional surgical procedure to provide a diagnosis and/or prognosis on a patient is necessarily invasive. Where a surgical probe is used to reduce the invasiveness, the procedure is often performed blindly or with indirect image guidance, with little accurate information on the location of the probe and/or whether the probe has located, navigated to or reached the target site. One result of a conventional approach is an increased number of false positive test results and false negative test results that directly affect the diagnostic results and the results of subsequent surgery at the target site. For example, about 37 percent of patients undergoing epidural anesthesia require three or more attempts at epidural placement. In another direction, about 20 percent of instances of prostate cancer are missed (false negative test result) by performance of a blind biopsy.

What is needed is a system and associated method that allows navigation to a target site and uses results from several different tests to identify a malignancy, a disease, a benign condition, a normal condition or any other medical condition (collectively referred to as "medical conditions" herein) at the target site from a reduced group of such conditions that may be present,

consistent with the data obtained from various measurements and other information. Preferably, the system should work with quantitative measurements, with qualitative measurements and with other relevant information on the subject and the subject's family. Preferably, the system should allow inclusion or exclusion of one or more selected measurements and information items without reconfiguration of the analysis of the data presented and should allow assignment of selected weights to different data items, corresponding to the importance of a data item in identifying presence of a particular medical condition.

Summary of the Invention

These needs are met by the invention, which provides an active system for measuring and determining the location, geometric parameters and medical condition(s) of a target site (organelle, cell, tissue, organ, etc.) within the body of an animal or a human being (collectively referred to herein as "animal"). The system relies upon measurements and other information from one or more of at least three types of sources: external measurements, from sources such as lymph node sampling, manual palpitation of the target site, mammograms, ultrasound scans, NMRI scans, CAT scans, estimation of target site size, surface roughness and/or calcification at the site and other similar functionalities; internal sensor measurements, including mechanical stiffness, thermal responsiveness, optical reflectance and imagery, target margin behavior, blood flow estimation, interstitial fluid pressure, vascular size, density and architecture, pH and electrical characteristics; and heuristic information involving prior medical history of the test subject and the subject's family.

Most or all of the measurements and information items are used to estimate the present location, present size and other geometric parameters, present medical condition and/or prognosis of the target site, by excluding or ruling out certain location and/or geometric parameters and/or other medical conditions. No one test determines the results. Most or all of the

measurements are used in combination to estimate the present medical condition of the target site.

Each internal measurement, external measurement and heuristic information item that lies in a selected range indicates possible presence of a group of medical conditions that is wholly, or largely, consistent with these data. In one approach, the set intersection of these different groups may be formed to provide a reduced group of medical conditions that is wholly, or largely, consistent with these measurements and information items.

Brief Description of the Drawings

Figure 1 is a schematic view of use of the system to sense a target site in a human's body according to the invention.

Figure 2 illustrates, in block diagram format, some of the four types of measurements used in practicing the invention.

Figure 3 graphically illustrates formation of a set intersection of groups of possible medical conditions according to the invention.

Figures 4A-4D graphically illustrate data and a result of analysis of these data according to the invention.

Figure 5 is a schematic view of a probe constructed according to the invention.

Figure 6 is a flow chart of a procedure to practice the invention.

Figure 7 is a schematic view of one approach to neural network modeling and processing of information provided by the invention.

Figures 8A and 8B are one-dimensional illustrations of a comparison of reference data points and observed data points according to the invention.

Description of Best Modes of the Invention

Figure 1 illustrates use of the invention to interrogate a target site 11 (organelle, cell, tissue, organ, etc.) in an animal body 13 according to one embodiment of the invention. A sensor or probe is inserted into the body 13 adjacent to the target site 11 and is activated to provide one or more internal measurements, which set forth in more detail in Figure 2. A region of the

body 13 adjacent to the target site is immobilized (to the extent this is possible) by a stereotactic or other body-holding device 15, and a sensor assembly or probe 17 is positioned adjacent to or within the target site, outside or inside the body. Internal measurements data are sensed or measured by the probe 17 and are received and stored by an internal data base 21. An internal data base 22, an external data base 23 and a heuristic database 25 hold internal measurements data external measurements data and heuristic information, respectively, also set forth in greater detail in Figure 2.

Figure 2 sets forth three kinds of data that are used to help determine one or more medical conditions of the target site 13: internal measurement sets, external measurements and heuristic information. Internal measurements include: (1) elasticity parameters of the target site and surroundings; (2) thermal parameters of the target site and surroundings; (3) optical reflectance of selected portions of, or all of, the target site surface and/or interior; (4) target margin characteristics for the target site; (5) estimates of blood flow within and/or adjacent to the target site; (6) vascular size, density and/pr architecture within and/or adjacent to the target site; (7) interstitial fluid pressure within and/or adjacent to the target site; (8) oxygen tension pO2 in a selected region within and/or adjacent to the target site; (9) pH of a selected region within and/or adjacent to the target site; (10) electrical parameters of a selected region within and/or adjacent to the target site; and (11) other relevant parameters.

Elasticity parameters include Young's modulus (resistance to strain imposed in a first direction when the body is unconstrained in any transverse direction), bulk modulus (resistance to change of three-dimensional volume), Poisson's ratio (change in dimension in a first direction in response to an imposed change in dimension in a second direction), and other similar parameters. One or more of the elastic parameters can be determined by observing a target site response to an abrupt step function force, to a slowly applied mechanical force and/or to a time varying force (such as a sinusoidal

force). For example, presence of a tumor at a target site may increase the Young's modulus by 400-900 percent, relative to the Young's modulus of a normal or healthy target site. No single parameter obtained from internal measurements is sufficiently specific that measurement and comparison of these parameter values with corresponding values for a "normal" target site will determine, by themselves, the nature of the abnormality present.

Thermal parameters include local temperature, thermal conductivity and specific heat capacity of a selected region adjacent to or within the target site. Specific heat capacity of a normal organ or tissue, for example, has an estimated range of about $c_p = 0.9 - 1$ cal/gm/^oC, whereas an organ or tissue that includes a tumor may have a higher range for c_p (reflecting the more "solid" nature of a tumor) or may have a lower range for c_p (reflecting the interrupted and irregular nature of blood flow, and thus temperature regulation, within a tumor). The temperature of a normal organ or tissue within a human may have a range T = 37-38 ^oC, whereas the temperature of an organ or tissue with certain diseases present may have a range several degrees Celsius higher.

Optical reflectance of a selected portion of, or all of, a target site is best evaluated by dividing a selected region of wavelengths λ, for example, 200 nm $\leq \lambda \leq$ 1200 nm, into wavelength bins of selected length $\Delta\lambda$, where $\Delta\lambda$ may be 10 nm - 100 nm, depending upon the medical condition being assessed. Optical reflectance OR(λ;meas), measured for the target site, is compared with "normal" optical reflectance OR(λ;normal) for each of a selected sequence of wavelength ranges to estimate whether the target site is abnormal, and if so, what is the group of medical conditions that presently affect the target site.

J. Mourant et al, in "Spectroscopic Diagnosis of Bladder Cancer With Elastic Light Scattering, Lasers in Surgery and Medicine, vol. 17 (1995) pp. 350-357, have examined ten patients with suspected bladder cancer, using one or more optical fibers to illuminate a region and another optical fiber to

collect the backscattered light in a wavelength range 250 nm $\leq \lambda \leq$ 900 nm. These optical biopsy results were compared with actual biopsies performed at the same sites. After subtracting a dark background that is common to all measurements at each of a sequence of wavelengths, these workers found that for 20 malignant regions, the normalized optical reflectance spectrum had a strong negative slope in the wavelength region 330 nm $\leq \lambda \leq$ 370, while 29 of 30 non-malignant regions had a normalized optical reflectance spectrum with a modest positive slope for the same wavelength region; the specificity for this test, based on the ten patients examined, is 97 percent.

Use of optical reflectance to serve as a guide in navigating a probe within brain tissue, and distinguishing white matter from gray matter therein, is reported by H. Liu et al in "Investigation of Optical Reflectance from Human Brain in vivo for Guiding Brain Surgery" [citation]. White matter reflectance is 3-5 times as large as gray matter reflectance in a wavelength region 600 nm $\leq \lambda \leq$ 800 nm, and this difference appears to extend to higher and lower wavelengths as well. A transition region near the gray-white matter boundary witin a brain has optical reflectances that are intermediate between the gray matter and white matter values.

The margins of certain tumors may have certain characteristics that differ from the corresponding characteristics for the core or interior of the tumor. For example, the increased interstitial fluid pressure in the core of a tumor drops sharply to that of a normal region near an edge of a tumor, as reported by P. Vaupel, in "Vascularization, blood flow, oxygenation, tissue pH, and bioenergetic status of human breast cancer", Oxygen Transport to Tissue, Plenum Press, New York, vol. 18 (1997), pp. 143-154, and discussed in greater detail in the following. Comparison of these characteristics for the margin(s) and for the core, using selected scanning or imaging techniques, may help distinguish between the presence and absence of certain kinds of tumors. The size of a margin or transition region may also indicate presence

of a non-normal target site. For example, a margin size for a well developed tumor is typically about 2.7 mm.

An estimate can be made of blood flow velocity adjacent to or within the target site using a sensor that estimates blood flow using a Doppler velocity sensor or similar indirect estimating procedures. For a normal breast, a breast with a benign tumor and a breast with a malignant tumor, measured mean blood flow values are 311 ± 157 flux units, 482 ± 209 flux units and 711 ± 280 flux units, respectively. Thus, larger than normal blood flow velocity appears to indicate presence of a benign or malignant tumor.

Where measured vascular density for a target site is higher, by a multiplicative factor of 2-10 or higher, than a normal range of vascular density (e.g., 2-3 per mm^2) for that site, this condition often indicates the presence of a malignant tumor. Comparison of measured vascular size with vascular size range for a normal target site (e.g., 0.2 mm) can indicate presence of a class of non-normal medical conditions (benign or malignant), especially if the measured size is at least 200 percent higher than the normal range of sizes.

P. Vaupel, op cit, notes that growth of an avascular, three-dimensional aggregate of tumor cells is self-limiting. The establishment of progressive expansion of malignant tumors is possible only if supply and drainage are initiated through blood flow through exchange vessels in a tumor bed, using pre-existing normal host blood vessels and using newly-formed tumor vessels arising from neovascularization. Angiogenesis, the formation of new capillaries from an existing vascular network, appears to be essential for tumor growth and metastasis, and some angiogenesis parameters (pO2, vascular count, vessel morphology, etc.) can also be used for prognosis. Greater vascular density may be associated with longer patient survival, although some other studies reach an opposite conclusion. A growing tumor is unable to form its own lymphatic system and must rely on other sources for blood, nutrients, oxygen, etc. Bulk flow of free fluid in interstitial spaces

appears to be much higher in a tumorous region than in a normal region: 15 percent of normal convective plasma flow for breast cancer regions versus 0.5-1 percent of normal convective plasma flow for a normal region. These increased interstitial fluid pressures drop sharply near the edge of a tumor

Interstitial fluid pressure (IFP) is a measure of a balance of fluid entering a target site and fluid exiting from the target site. Only an invasive breast tumor has a consistently higher IFP value (15-32 mm Hg) than does a normal or healthy breast (-0.4 to +4 mm Hg), where an IFP measurement needle tip is located within the tumor region. The results reported in the preceding paragraph by Vaupel, op cit, are also relevant here.

Comparison of oxygen tension pO2 (or PPO) for a selected region adjacent to or within the target site with corresponding values for a normal target site can provide an indication of whether or not a particular class of medical conditions is present. Vaupel, Kallinowski and Okunieff, in "Blood Flow, Oxygen and Nutrient Supply, and Metabolic Microenvironment of Human Tumors; A Review", [citation] report on a study of change of pO2 in cervical mucosa with progress of cervical cancer. In a normal, non-cancerous cervix, the the pO2 median value is 36 mm Hg. For stages 0, 1 and 2 of cervical cancer, the pO2 median value drops to 20 mm Hg, to 13 mm Hg and to 5 mm Hg, respectively. The measured pO2 value appears to move to lower and lower values as cancer progresses, as compared to a normal or healthy range for the cervix. A non-metastasising breast tumor ($pO2 \approx 20$ mm Hg) has a larger mean pO2 value than does a metastasising breast tumor ($pO2 \approx$ 7.5 mm Hg). Based on other measurements reported, a tumor growing in association with an organ appears to require at least 50 percent more oxygen than a normal organ, and this may be manifested by a much smaller pO2 value where a tumor is present.

Results reported by Vaupel, op cit, on oxygen consumption in a breast cancer tumor (3-10 μl/gm/min) versus oxygen consumption in a normal region (3-6 μl/gm/min) are consistent with these results. Hypoxia is present in

many tumorous regions. Vaupel found pO2 values of 0-2.5 mm Hg for breast tumors and pO2 values of at least 12.5 mm Hg for normal regions. A bimodal pO2 distribution is often manifested, indicating presence of normal and hypoxic regions side by side.

The pH of a selected region adjacent to or within a target site can be measured and compared with a normal range of pH for the target site, as an indicator of the possible presence of one or more of a class of medical conditions. A normal target site will have a steady state pH of 7-7.4, reflecting the corresponding values of blood pH. Extracellular pH has a mean value of 7.35 for a normal target site and 7.0 for a tumorous target site. Intracellular pH has a mean value of 7.04 for a normal target site and 7.2 for a tumorous target site. For a tumorous cell, pH(intracellular) is significantly greater than pH(extracellular). However, mislocation of the site of measurement of pH (inside versus outside a cell) may lead to a wrong conclusion concerning the condition of the cell or target site.

Vaupel, op cit, reports that the intracellular pH is neutral to mildly alkaline for tumorous cells that are not deprived of oxygen or energy, while the extracellular pH is acidic. This cross-membrane gradient for a tumorous cell is opposite in sign to the cross-membrane gradient for a normal cell, where pH(intracellular) is lower than pH(extracellular).

A.J. Surowiec et al, in I.E.E.E. Trans. on Biomedical Engineering, vol. 35 (1988) pp. 257-262, report on measurements of dielectric parameters at frequencies up to 100 MHz. These workers find that electrical conductivity in tumorous breast tissue is 100-200 percent higher than electrical conductivity in normal breast tissue: 2-3 mS/cm versus about 1 mS/cm. Other tissues are believed to be similarly affected by changes in structure and composition, due to cell proliferation and tumor growth, and similar differences in electrical conductivity and other dielectric parameters is expected for other tissues.

The sensor assembly and probe 17 can also be used to assist the probe in navigating to the target site, preferably in real time. One approach here

uses general shapes, assumed to be known, and imaging of the organs and major tissue groups to move the probe to a location adjacent to the target site. At this location, the probe can perform certain internal measurements outside the target site, before the probe is moved within the probe site for additional measurements.

Data from external measurements, not relying upon measurements taken with the sensor assembly and probe 17, may also help limit the class of medical conditions, if any, present at the target site. One example is data extracted from mammogram imaging performed on an adult female. This image may: (1) indicate the likely presence of a particular disease (e.g., cancer of the breast); (2) be consistent with, but not unambiguously indicate the presence of, a particular disease; or (3) may be inconsistent with, or be contra-indicative of, the presence of a particular disease. Another example is a protein specific antigen (PSA) test, performed on an adult male, to detect the (increasing) likelihood of presence of prostate cancer.

Another class of external measurements are the NMRI scans, CAT scans, ultrasound scans and mammograms, which provide data on or adjacent to a target site that can be compared with data from measurements on normal target sites.

Another class of external measurements are lymph node samples, which may indicate presence of a normal medical condition or of a precursor or a vestige of a non-normal medical condition, such as HIV, that is not yet present, or is no longer present, at other sites within a body.

Another class of external measurements involve simple manual palpitation of a region of a body and comparison of the response with an expected response from a normal, undiseased body.

The size and/or shape of a target site can be estimated, using scanning or imaging (NMRI or ultrasound), or using a sequence of two or more measurements, taken at different locations relative to the target site, and some

analytical geometry computations to estimate the parameters of an ellipse that approximately coincides with the target site, as discussed in the following.

The roughness (spiculation) of a target site surface can be estimated using an NMRI scan or ultrasound scan. Spiculation associated with a boundary of a tumorous target site may differ significantly from spiculation of an adjacent normal site. This difference should be evident from the results of an NMRI scan or ultrasound scan, if the region interrogated can be made smaller than the present size of a tumor.

A measurement or other estimate of the amount of calcification associated with a target site can be estimated, using optical imaging, NMRI scanning, ultrasound scanning or (preferably) a mammogram, and can be compared with the amount and pattern of calcification associated with a normal or benign target site to determine whether a class of medical conditions is likely to be present.

Size, surface roughness and calcification associated with a target site are (somewhat arbitrarily) treated as external measurements because these parameters are often obtained using NMRI and/or ultrasound scanning to provide the data. However, one or more of these information items could also be treated as an internal measurement.

Heuristic information, including but not limited to medical history of the subject and of the subject's family, may be used to provide an indicator of consistency or inconsistency of an extant prognosis determined from internal and/or external measurements. For example, the subject's family may have an extensive medical history of cancer involving a particular group of organs (e.g., breast, prostate and colon), which should be taken into account in any diagnosis or prognosis at a target site.

The external measurements and the heuristic information provide data that are often not directly and numerically comparable with corresponding data for a normal target site. The external measurements data and/or heuristic information are preferably analyzed using a fuzzy logic interface that does

not rely upon comparison of numerical values but that can return a (fuzzy) determination that it is more likely that not that a particular medical condition is, or is not, present. For example, comparison of a calcification pattern for an observed target site with a calcification pattern for a corresponding normal target site may be performed visually and subjectively by a health care professional and/or may be performed by a software algorithm, relying upon fuzzy logic and the nature of the pattern differences rather than upon a hard-edged comparison of one or more numerical parameters for the patterns. Fuzzy logic is discussed by B. Kosko and S. Isaka in "Fuzzy Logic", Scientific American, July 1993, pp. 78-81.

Data from any of the preceding N1 = 10 groups of internal measurements, from the N2 = 7 groups of external measurements and/or from the N3 = 2 groups of heuristic information are preferably analyzed using a direct interface with analytical software that is part of the system. Some of these numerical data may be directly compared with corresponding numerical ranges to determine whether a particular medical condition is likely to be present at the target site. Each group of internal measurement data, each group of external measurement data and each group of heuristic information items provides a more or less independent dimension in a "medical condition space" of dimension N1+N2+N3. Preferably, each medical condition that is present in, or is wholly or largely consistent with, the measurements in each of these dimensions has an associated confidence level, with values ranging from 0 percent to 100 percent.

Presence of a medical condition, especially a non-normal one, in each of two or more such dimensions affirmatively indicates the possible presence of that medical condition, as discussed in the preceding. When this occurs, an initial diagnosis uses the set intersection of the medical conditions in each dimension to provide a list of medical conditions that is consistent with the medical conditions present in each dimension. Figure 3 graphically illustrates provision of a reduced group of medical conditions from intersection of

groups numbered 1, 3 and 7 of the internal measurement data and group number 2 of the external measurement data, as an example.

Internal measurement data, external measurement data and heuristic information are preferably analyzed using a neural network that is configured as discussed in the following.

Figures 4A, 4B and 4C graphically illustrate certain quantitative external measurement data that might be obtained for a target site at which a tumor may be present, indicating target site size (Figure 4A), spiculation (Figure 4B) and shape (Figure 4C). Figure 4D indicates a possible result of analysis of the results obtained from the data shown in Figures 4A, 4B and 4C. In this instance, the confidence level that the target site includes a malignant tumor is about 25 percent, which may be large enough to warrant performance of more invasive exploratory and corrective surgery.

Figure 5 is a schematic view of a sensor assembly and probe 17 including mechanisms to perform measurements associated with each of the ten types of internal measurements discussed in the preceding. A first probe mechanism 17-1 measures one or more elastic parameters associated with the target site, preferably including at least one of Young's modulus and bulk modulus. A second probe mechanism 17-2 measures one or more thermal parameters, drawn from a group consisting of local temperature and specific heat capacity associated with the target site. A third probe mechanism 17-3 measures optical reflectance OR(λ;meas) of a selected region of the target site for one or more selected wavelength ranges. A fourth probe mechanism 17-4 measures one or more characteristics of the margin of a target site. A fifth probe mechanism 17-5 measures amount of blood flow adjacent to or within the target site. A sixth probe mechanism 17-6 measures vascular size and/or vascular density associated with the target site. A seventh probe mechanism 17-7 measures interstitial fluid pressure associated with the target site. An eighth probe mechanism 17-8 measures oxygen tension pO2 associated with the target site. A ninth probe mechanism 17-9 measures local pH associated

with a selected portion of the target site. A tenth probe mechanism 17-10 measures one or more electrical parameters associated with a selected portion of the target site. One or more of these probe mechanisms can be included in the probe; and one or more of these probe mechanisms can be included in each of two probes that cooperate to sense and measure various internal data for comparison. Optionally, the probe 17 may also be configured to measure one or more parameters associated with size, shape, surface roughness and/or calcification pattern associated with a target site.

Figure 6 is a flow chart of a procedure for practicing the invention. In step 61 (optional), an internal probe is used to aid in navigation of the probe to a target site (e.g., using optical reflectance of organs and/or tissues along a path to the target site), with appropriate confidence levels incorporated. In step 63, two or more internal measurements are performed at the target site using the probe, with appropriate confidence levels incorporated. In step 65 (optional), one or more external measurements are performed at the target site, with appropriate confidence levels incorporated. In step 67 (optional), one or more heuristic information items concerning the target site are included, with appropriate confidence levels incorporated. In step 69, a group of one or more medical conditions, each of which is generally consistent with the internal measurements, with the (optional) external measurements, and with the (optional) heuristic information items, is provided. In some instances, an internal measurement, an external measurement and/or a heuristic information item that is inconsistent with the remainder of the data for the target site may be either ignored or given much smaller weight, or even negative weight, in determining this group of medical conditions. In step 71, at least one medical condition from the provided group is identified as likely to be present for the test subject.

One approach to processing and analyzing the results of comparison of one or more internal measurements at a target site with selected reference values corresponding to a normal or benign medical condition, or

corresponding to a malignant (tumorous) medical condition, is through neural net processing. At least two alternatives are available: radial basis neural net modeling and backpropagation modeling.

Radial basis neural net modeling ("NNM") is summarized in Neural Network Toolbox For Use With Matlab, The Math Works, Third Version, 1998, pp. 6-1 through 6-19, and is characterized in Figure 7. This neural network includes three layers, an input layer 81, one or more hidden layers 83, and an output layer 85. The input layer 81 accepts an input vector **p**, forms a difference between the vector **p** and an input weight vector **w**, optionally multiplies the difference **p** - **w** by a selected bias or sensitivity vactor **b** to form a scalar product, and passes this scalar product to an intermediate layer for further processing and analysis.

The dimension N of the vectors **p** and **w** may be the total number of independent internal measurements plus independent external measurements plus heuristic information items presented for the test subject. For example, if three internal measurement sets (1, 3, 7), one external measurement set (4) and one heuristic information item (1) are presented, as in Figure 3, the dimension N = 3 + 1 + 1 = 5. More likely, the dimension N will be a larger number, in order to obtain discrimination between two medical conditions having similar data for "lower dimensional" measurements.

The radial basis neural network ("RBNN"), shown schematically in Figure 7, will produce an output value OUT that is close to zero, if the vectors **p** and **w** differ substantially from each other and will produce an output value OUT $\approx$ 1 if the vectors **p** and **w** are (nearly) equal to each other. One object of processing by an RBNN is to identify an input vector **p** that provides an output value that is close to, or equal to, 1 for one or more of a selected sequence of input weight vectors **w**. In this RBNN analysis, more than one input weight vector **w** may be used at the same time.

Consider an R-dimensional space S having a finite collection of Q reference data points therein, each with coordinates $\mathbf{x}(q) = (xq1, xq2, \ldots, xqR)$ $(q = 1, 2, \ldots, Q)$, with each point in this collection representing a reference data point with an associated medical condition for a selected target site. The data represented by the point $\mathbf{x}(q)$ are taken from certified observations made on one or more reference test subjects and include data from internal measurements, from external measurements and from heuristic information on medical condition of the target site. Preferably, each R-dimensional space S is associated with a different target site (brain, heart, liver, pancreas, kidney(s), intestines, lung(s), thorax, selected tissues, selected groups of cells associated with a given organ, etc.) for the reference test subjects. Each reference data point $\mathbf{x}$ is associated with one of K=2 medical conditions for the target site: malignant (M) or normal/benign (B). More generally, each reference data point $\mathbf{x}$ is associated with one of K (≥ 2) selected medical conditions for the target site.

Assume that a patient (a non-reference test subject) is subjected to probing with the probe and/or scanning according to the invention for a selected target site and that internal and/or external measurements produce at least one observed data point $\mathbf{y} = (y1, y2, \ldots, yR)$ in the space S. The distances $\{d(\mathbf{x}(q);\mathbf{y})\}$ $(q = 1, 2, \ldots, Q)$ are compared with each other, and at least one reference data point $\mathbf{x}(q0)$ satisfies

$$d(\mathbf{x}(q0);\mathbf{y}) = \min_q\{d(\mathbf{x}(q);\mathbf{y})\}. \qquad (1)$$

The distance $d(\mathbf{x}(q);\mathbf{y})$ may be defined generally as

$$d(\mathbf{x}(q);\mathbf{y}) = \{\sum_{r=1}^{R} w_r\,|xqr - yr|^s\}^{1/s}, \qquad (2)$$

where w_r is a selected non-negative weight value and s is a selected positive number. The choice $\{w_r = 1, s = 2\}$ recovers the conventional Euclidean distance metric. A more general distance metric $d(\mathbf{x}(q);\mathbf{y})$ may also be used

here that satisfies three standard requirements for a metric: (1) $d(\mathbf{x},\mathbf{y}) \geq 0$, (2) $d(\mathbf{x},\mathbf{y}) = d(\mathbf{y},\mathbf{x})$ and (3) $d(\mathbf{x},\mathbf{z}) + d(\mathbf{z},\mathbf{y}) \geq d(\mathbf{x},\mathbf{y})$.

Assume, for definiteness, that a reference data point $\mathbf{x}(M1)$, belonging to the malignant set M, is found to be closest to the observed data point $\mathbf{y}$ so that $\mathbf{x}(q0) = \mathbf{x}(M1)$ satisfies the relation (1). For illustrative purposes, the two next-nearest reference data points are assumed to be $\mathbf{x}(B1)$ and $\mathbf{x}(B2)$, belonging to the normal/benign set (referred to collectively as the "normal" set) B. For purposes of initial illustration, the dimension of the space S is assumed to be R=1 in Figure 8A so that the space is a line segment, having a single coordinate y, with each reference data point having a location on that line segment.

Observed data points y that are "close to" a reference data point, such as x(M1), on this line segment will have a correspondingly high overall probability Pr[y] that the medical condition of the target site belongs to the malignant set M. Observed data poiints on this line segment that are "close to" a reference data point, such as x(B1) or x(B2), on this line segment will have a correspondingly high overall probability that the medical condition of the target site belongs to the normal set B. A probability function

$$Pr(\mathbf{x}(q);\mathbf{y}) = F(d(\mathbf{x}(q);\mathbf{y});q) \qquad (3)$$

is assigned to each of the Q reference data points, where F is a monotonically decreasing (preferably continuous) function of the distance $d(\mathbf{x}(q);\mathbf{y})$ between the observed data point $\mathbf{y}$ and the reference data point $\mathbf{x}(q)$. Each function F satisfies $0 \leq F \leq 1$ and may vary with the index q as well. In one version of the first and second embodiments, the probability function $F(d(\mathbf{x}(q);\mathbf{y});q)$ is the same for all reference data points $\mathbf{x}(q)$ belonging to a malignent medical condition set (M) and is the same for all reference data points $\mathbf{x}(q)$ belonging to a normal medical condition set (B). Use of a probability function F that varies more generally with the index q complicates the analysis but can be incorporated. Suitable classes of probability functions F include exponential

$$F(d(\mathbf{x};\mathbf{y})) = \exp\{-\alpha \cdot d(\mathbf{x};\mathbf{y})^p\}, \qquad (4A)$$

inverse polynomial

$$F(d(\mathbf{x};\mathbf{y})) = \alpha/\{\beta + \chi \cdot d(\mathbf{x};\mathbf{y})^p\}, \quad (4B)$$

and linear or nonlinear

$$F(d(\mathbf{x};\mathbf{y})) = \alpha - \beta \cdot \{d(\mathbf{x};\mathbf{y})^p\}, \quad (4C)$$

where α, β, χ and p are selected real numbers.

If the reference data point $\mathbf{x}(q)$ corresponds to a malignant medical condition (or to a normal medical condition), $F(d(\mathbf{x}(q);\mathbf{y});q)$ corresponds to a probability that the observed data point is indicative that the observed data point belongs to the set M (or to the set B). Figure 8B graphically illustrates, in one dimension, three typical probability functions for the reference data points B1, M1 and B2. Note that, for example, the probability functions corresponding to B1, to B2 and to M1 need not be the same. The one-dimensional situations illustrated in Figures 8A and 8B are easily generalized to R dimensions, using the distance metric $d(\mathbf{x}(q);\mathbf{y})$. The relative positions of the data points B1, B2 and M1 may be changed as long as at least one normal data point (B1 or B2) and at least one malignant data point (M1) are present.

In one embodiment, the overall probability associated with the target site (represented by the observed data point y) is

$$Pr[\mathbf{y}] = \max_q F(d(\mathbf{x}(q);\mathbf{y});q), \quad (5)$$

and the corresponding medical condition for the target site is the medical condition for the reference data point(s) $\mathbf{x}(q0)$ satisfying Eq. (1), denoted herein as $MC(\mathbf{x}(q0))$. In the one-dimensional illustration in Figure 8B, the overall probability would be determined by

$$\begin{aligned} PR[y] &= F(d(x(B1);y) \quad (y \le x_{B1,M1}) \\ &= F(d(x(M1);y) \quad (x_{B1,M1} < y < x_{M1,B2}) \\ &= F(d(x(B2);y) \quad (y \ge x_{M1,B2}), \end{aligned} \quad (6)$$

where $x_{B1,M1}$ is the value of y at which F(d(x(B1);y) and F(d(x(M1);y) are equal and $x_{M1,B2}$ is the value of y at which F(d(x(M1);y) and F(d(x(B2);y) are equal.

If, for a given observed data point y, J reference data points **x**(q0j) (j = 1, ... , L) are found that satisfy Eq. (1), with $J \geq 1$, a modified overall probability Pr[**y**}/J is assigned to each of the medical conditions associated with the data points **x**(q0j). Where all J medical conditions are the same, that medical condition is assigned an overall probability of Pr[**y**] for the target site. Where two (or more) different medical conditions occur, denoted as MC(**x**(q0j1)) and MC(**x**(q0j2)) for definiteness, corresponding to different reference data points that each satisfy Eq. (1), a modified overall probability assigns a portion of the probability PR[**y**], defined in Eq. (5) to each of the medical conditions MC(**x**(q0j1)) and MC(**x**(q0j2)).

In a second embodiment, given the observed data point **y**, a first nearest-neighbor reference data point **x**(q01) and a second nearest-neighbor reference data point **x**(q02), corresponding to a malignant medical condition and to a normal medical condition, respectively, are identified, with corresponding probability functions as defined in Eq. (3). The probability that the target site is malignant and the probability that the target site is normal are then taken to be

$$Pr(\mathbf{y} \varepsilon M) = F(d(\mathbf{x}(q1);\mathbf{y});q1)/(Sum) \tag{7}$$

and

$$Pr(\mathbf{y} \varepsilon B) = F(d(\mathbf{x}(q2);\mathbf{y});q2)/(Sum), \tag{8}$$

respectively, with

$$Sum = F(d(\mathbf{x}(q1);\mathbf{y});q1) + F(d(\mathbf{x}(q2);\mathbf{y});q2). \tag{9}$$

The definitions (7), (8) and (9) ensure that the sum of the probabilities for the two independent events {**y** ε M} and {**y** ε B} is non-negative and is no greater than 1.0. The definitions (7), (8) and (9) extend to a situation where more than one reference data point **x**(q) ε M satisfies Eq. (1) and/or where more than one reference data point **x**(q) ε B satisfies Eq. (1).

Each of the first and second embodiments extends from dimension R = 1 to any higher integer dimension R. Other formulations of the overall probability Pr[**y**] associated with the observed data point **y** can also be used

here. This analysis can be combined with an RBNN approach to train a network and to assign probabilities to different medical conditions at a target site, based on comparison of observed and reference data points.

Another useful neural net modeling technique is backpropagation, wherein NN input vectors and NN output vectors are analyzed and used to train a network to associate specific input vectors with specific output vectors and to associate NN input vectors in a desired manner. Standard backpropagation uses a gradient descent analysis, using a conjugate gradient , Newton or other suitable approach. The backpropagation method is summarized in Neural Network Toolbox For Use With Matlab, The Math Works, Third Version, 1998, pp. 5-1 through 5-56.

What is claimed is:

1. A system for performing one or more relevant measurements at a target site in an animal body, the system comprising:

a probe that can be inserted into a body adjacent to or within a target site and that comprises at least one of:

a first probe mechanism that measures one or more elastic parameters associated with the target site drawn from a group consisting of a Young's modulus, a bulk modulus and a Poisson's ratio associated with the target site;

a second probe mechanism that measures one or more thermal parameters, drawn from a group consisting of local temperature, thermal conductivity and specific heat capacity associated with the target site;

a third probe mechanism that measures optical reflectance OR(λ;meas) of a selected region of the target site for one or more selected wavelength ranges;

a fourth probe mechanism that measures a selected characteristic of a margin of the target site;

an fifth probe mechanism that measures amount of blood flow adjacent to or within the target site;

a sixth probe mechanism that measures interstitial fluid pressure adjacent to or within the target site;

a seventh probe mechanism that measures vascular size and/or vascular density associated with the target site;

an eighth probe mechanism that measures oxygen tension pO2 associated with the target site;

a ninth probe mechanism that measures local pH associated with a selected portion of the target site; and

a tenth probe mechanism that measures at least one electrical parameter associated with a selected portion of the target site; and

a database and analyzer that receives and compares each measurement made by the probe with a corresponding range of values that is representative of a normal target site and, for each probe measurement that does not fall within the corresponding range of values for a normal target site, the database and analyzer provides at least one medical condition of the target site that is generally consistent with the probe measurement.

2. The system of claim 1, wherein said at least one probe measurement is combined with at least one additional measurement that is drawn from a group of measurements, performed adjacent to or within said target site, consisting of lymph node samples, mammograms, ultrasound scans, NMRI scans, CAT scans, estimation of target site size, estimation of target site shape, estimation of target site surface roughness and estimation of calcification.

3. The system of claim 1, wherein at least one probe measurement is combines with at least one additional information item that is drawn from a group consisting of (1) at least one medical condition that said animal has exhibited and (2) at least one medical condition that a family member of said animal has exhibited.

4. The system of claim 1, wherein, when each of at least two of said probe mechanisms provides a measurement value that does not fall within said corresponding range of values for said normal target site, said database and analyzer provides at least one disease or malady of said target site that is consistent with each of the at least two probe mechanism measurements.

5. The system of claim 1, wherein said analyzer comprises a neural net device that receives and processes said measurement from said at least one probe mechanism and provides a processed measurement value that can be compared with said corresponding range of values for said normal target site.

6. The system of claim 5, wherein said neural net device performs a radial basis neural network analysis.

7. The system of claim 5, wherein said neural net device performs a backpropagation neural network analysis.

8. The system of claim 1, wherein at least one of said probe mechanisms is used to navigate said probe to a location adjacent to or within said target site.

9. A method for performing one or more relevant measurements at a target site in an animal body, the method comprising:

providing a probe that can be inserted into a body adjacent to or within a target site and that comprises at least one of:

a first probe mechanism that measures one or more elastic parameters associated with the target site drawn from a group consisting of a Young's modulus, a bulk modulus and a Poisson's ratio associated with the target site;

a second probe mechanism that measures one or more thermal parameters, drawn from a group consisting of local temperature, thermal conductivity and specific heat capacity associated with the target site;

a third probe mechanism that measures optical reflectance OR(λ;meas) of a selected region of the target site for one or more selected wavelength ranges;

a fourth probe mechanism that measures a selected characteristic of a margin of the target site;

an fifth probe mechanism that measures amount of blood flow adjacent to or within the target site;

a sixth probe mechanism that measures interstitial fluid pressure adjacent to or within the target site;

a seventh probe mechanism that measures vascular size and/or vascular density associated with the target site;

an eighth probe mechanism that measures oxygen tension pO2 associated with the target site;

a ninth probe mechanism that measures local pH associated with a selected portion of the target site; and

a tenth probe mechanism that measures at least one electrical parameter associated with a selected portion of the target site; and

providing a database and analyzer, including a computer that is programmed to receive and compare each measurement made by the probe with a corresponding range of values that is representative of a normal target site and, for each probe measurement that does not fall within the corresponding range of values for a normal target site, the database and analyzer provides at least one disease or malady of the target site that is consistent with the probe measurement.

10. The method of claim 9, further comprising combining said at least one of said probe measurements with at least one additional measurement, performed adjacent to or within said target site, consisting of lymph node samples, mammograms, ultrasound scans, NMRI scans, CAT scans, estimation of target site size, estimation of target site shape, estimation of target site surface roughness and estimation of calcification.

11. The method of claim 9, further comprising combining at least one of said probe measurements with at least one additional information item that is drawn from a group consisting of (1) at least one medical condition that said animal has exhibited and (2) at least one medical condition that a family member of said animal has exhibited.

12. The method of claim 9, further comprising:

when each of at least two of said probe mechanisms provides a measurement value that does not fall within said corresponding range of values for said normal target site, said computer is programmed to provide at least one disease or malady of said target site that is consistent with each of the at least two probe mechanism measurements.

13. The method of claim 9, further comprising providing said analyzer with a neural net device that receives and processes said measurement from said at least one probe mechanism and provides a processed measurement value that can be compared with said corresponding range of values for said normal target site.

14. The method of claim 13, further comprising choosing said neural net device to perform a radial basis neural network analysis.

15. The method of claim 13, further comprising choosing said neural net device to perform a backpropagation neural network analysis.

16. The method of claim 9, further comprising using at least one of said probe mechanisms to navigate said probe to a location adjacent to or within said target site.

Abstract of the Invention

System and method for performing one or more relevant measurements at a target site in an animal body, using a probe. One or more of a group of selected internal measurements is performed at the target site, is optionally combined with one or more selected external measurements, and is optionally combined with one or more selected heuristic information items, in order to reduce to a relatively small number the probable medical conditions associated with the target site. One or more of the internal measurements is optionally used to navigate the probe to the target site. Neural net information processing is performed to provide a reduced set of probable medical conditions associated with the target site.

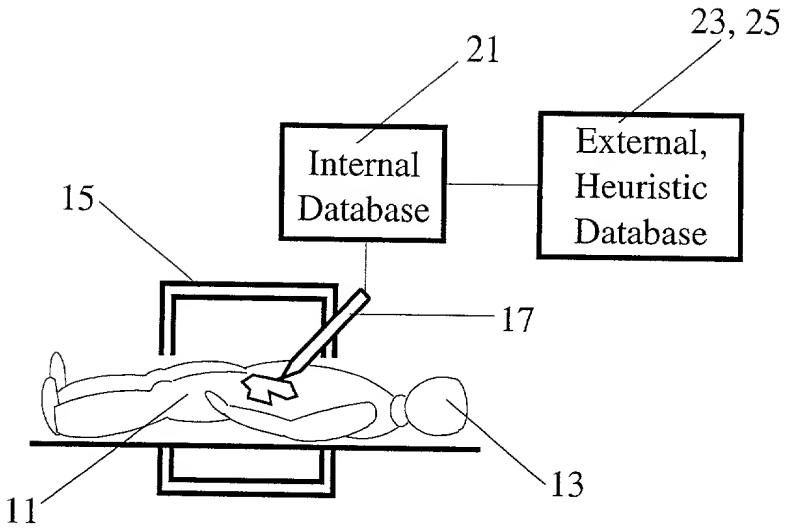
23, 25
21
Internal Database
External, Heuristic Database
15
17
11
13

FIG. 1

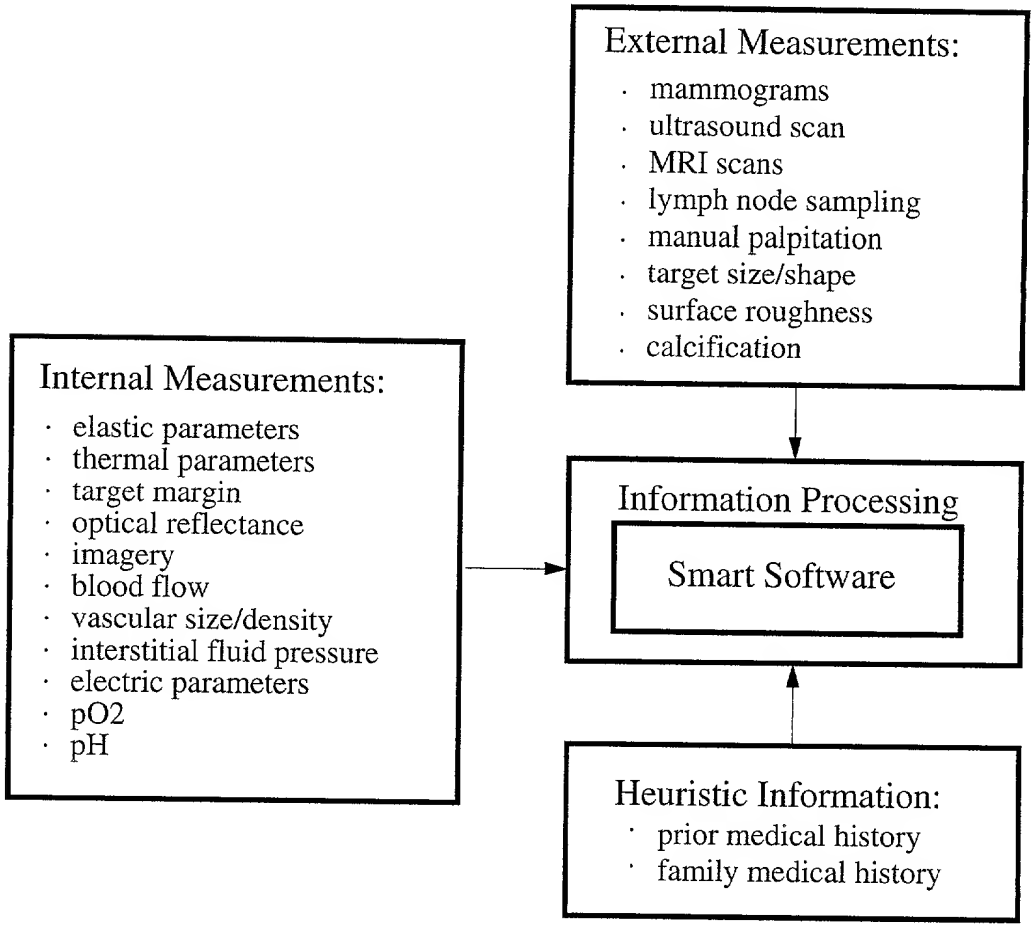
External Measurements:
· mammograms
· ultrasound scan
· MRI scans
· lymph node sampling
· manual palpitation
· target size/shape
· surface roughness
· calcification
Internal Measurements:
· elastic parameters
· thermal parameters
· target margin
· optical reflectance
· imagery
· blood flow
· vascular size/density
· interstitial fluid pressure
· electric parameters
· pO2
· pH
Information Processing
Smart Software
Heuristic Information:
· prior medical history
· family medical history

FIG. 2

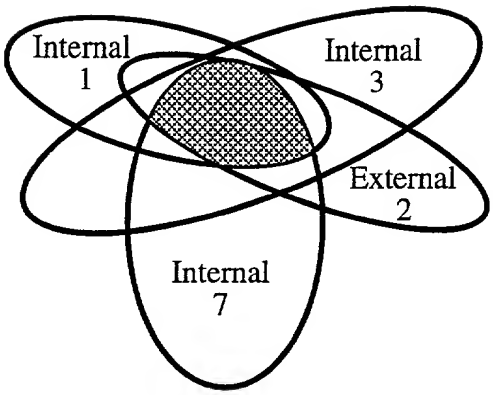
Internal
1
Internal
3
External
2
Internal
7

FIG. 3

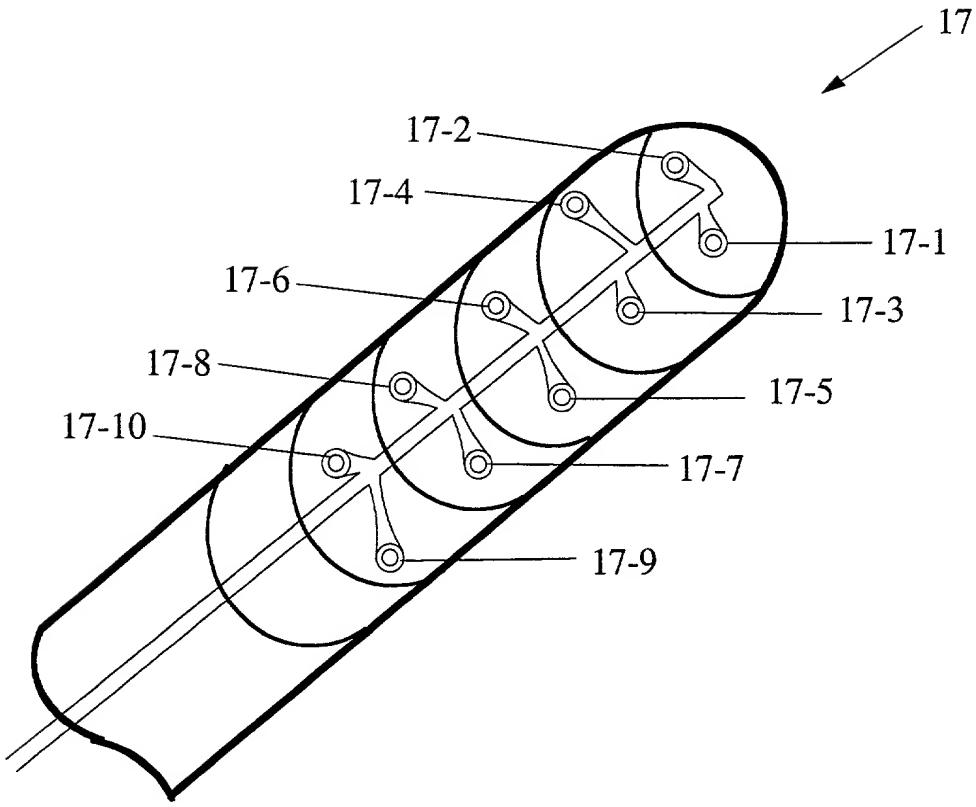
17
17-2
17-4
17-1
17-6
17-3
17-8
17-5
17-10
17-7
17-9

FIG. 5

Tumor size is 'very large'

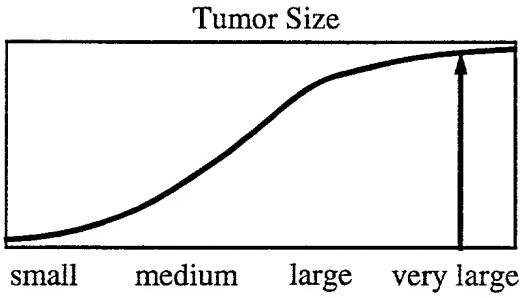

FIG. 4A

Tumor spiculation is 'very sharp'

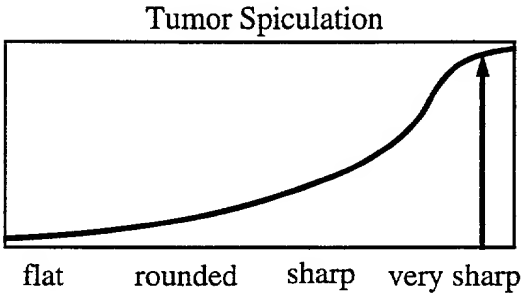

FIG. 4B

Tumor 3D shape is 'moderately concave'

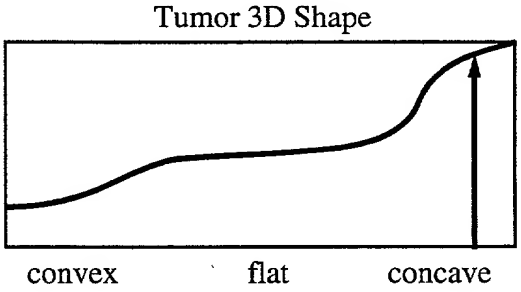

FIG. 4C

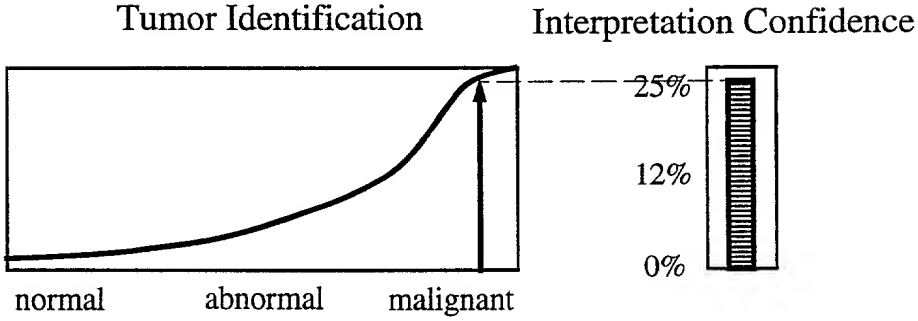

FIG. 4D

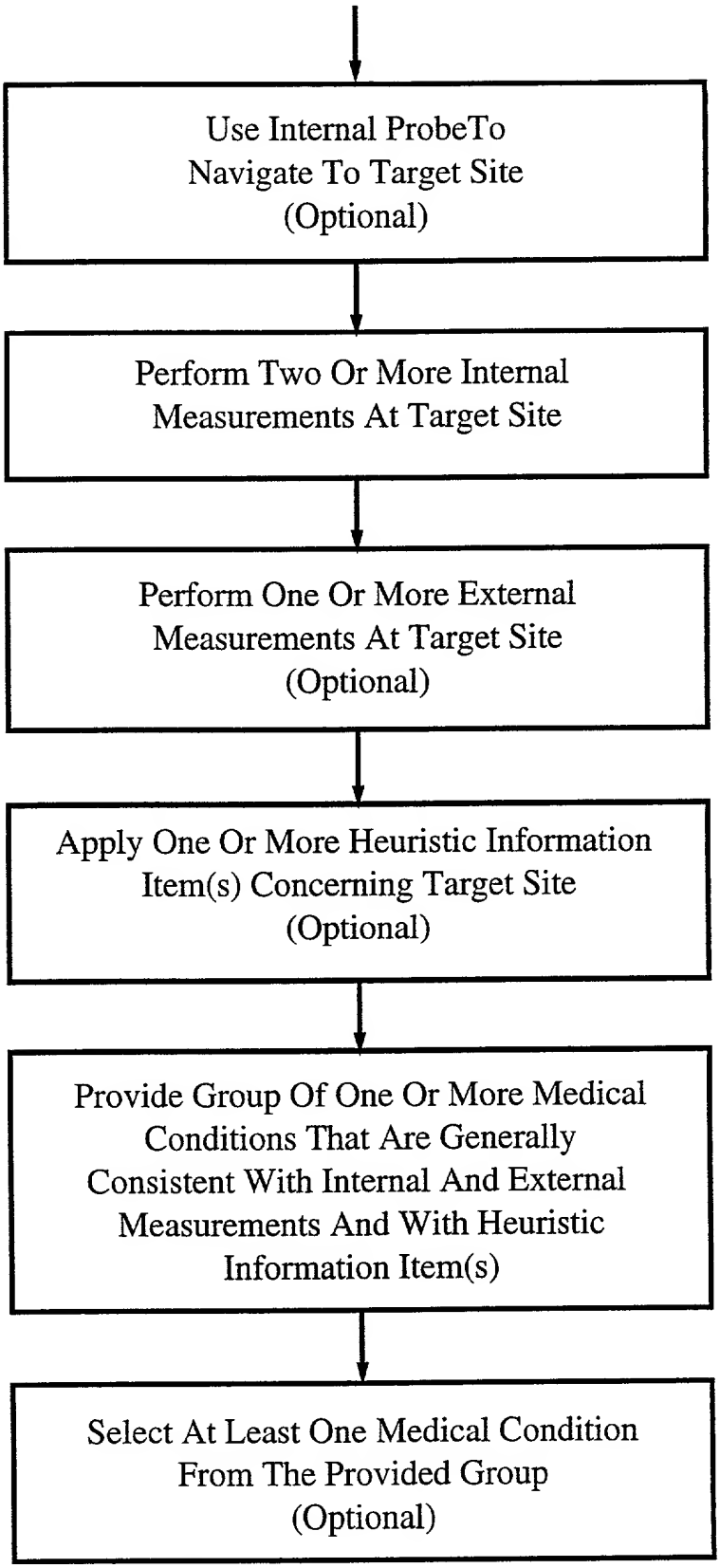
Use Internal ProbeTo Navigate To Target Site (Optional)
Perform Two Or More Internal Measurements At Target Site
Perform One Or More External Measurements At Target Site (Optional)
Apply One Or More Heuristic Information Item(s) Concerning Target Site (Optional)
Provide Group Of One Or More Medical Conditions That Are Generally Consistent With Internal And External Measurements And With Heuristic Information Item(s)
Select At Least One Medical Condition From The Provided Group (Optional)

FIG. 6

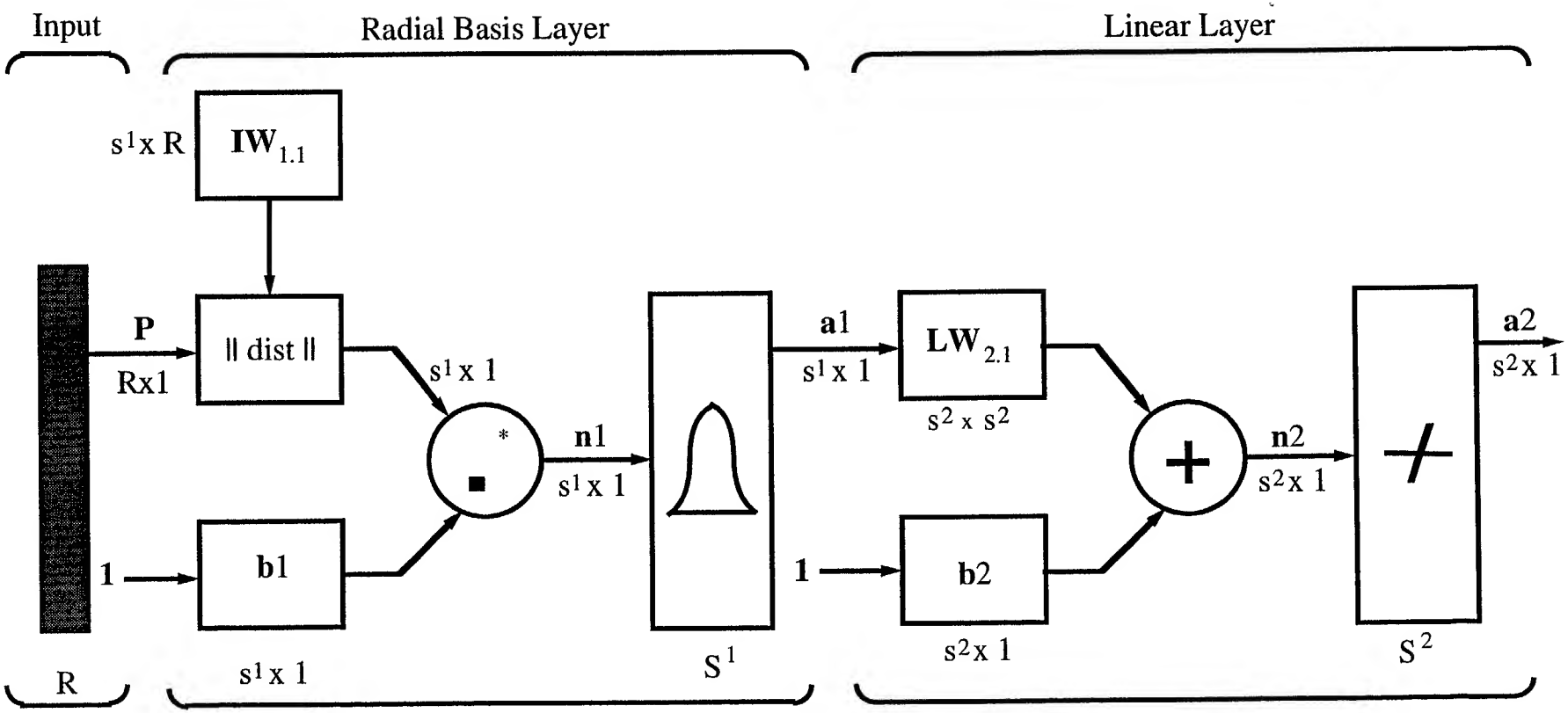
Input
Radial Basis Layer
Linear Layer
s1 x R
IW1.1
P
Rx1
|| dist ||
s1 x 1
n1
s1 x 1
a1
s1 x 1
LW2.1
s2 x s2
n2
s2x 1
a2
s2x 1
1
b1
s1x 1
1
b2
s2x 1
R
s1x 1
S1
S2

FIG. 7

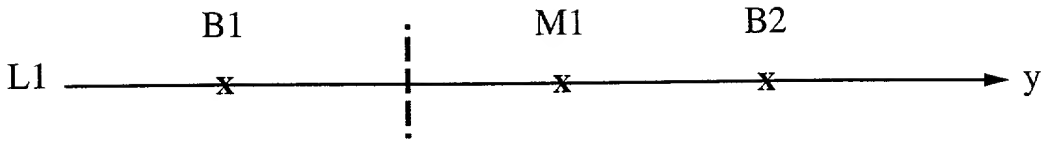

FIG. 8A

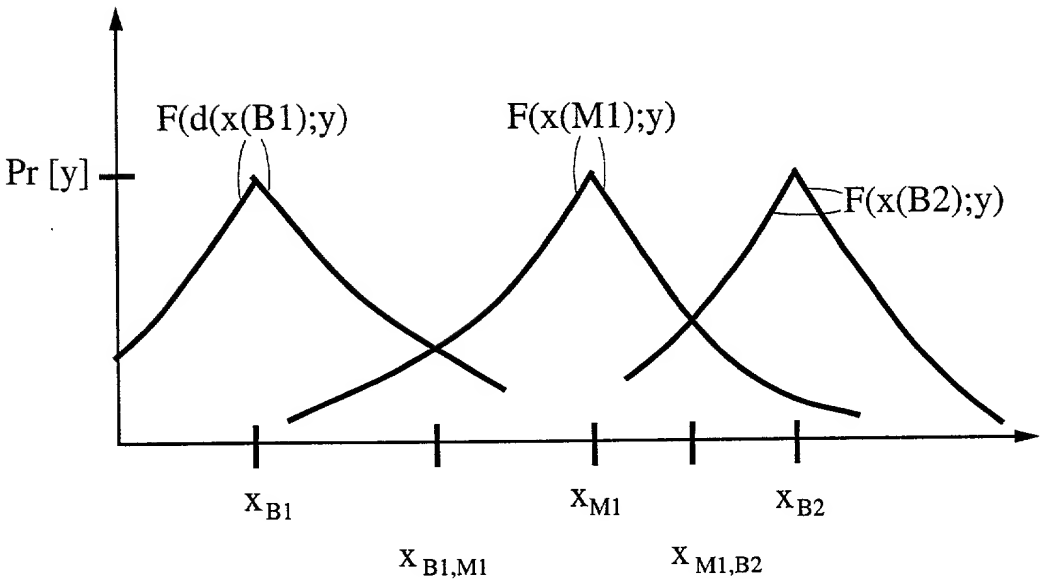

FIG. 8B

EK380732495US

NASA
National Aeronautics and Space Administration

Declaration, Power of Attorney and Petition Original Application

ARC-14231-2
(NASA Case No.)

As a below named inventor, I hereby declare that: my residence, post office address and citizenship, are stated below next to my name, I believe I am the original, first and sole inventor(if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Body Sensing System

the specification, of which ☒ is attached hereto, ☐ was filed on (date) _____ as

Application Serial No. _____ and was amended on (date) _____

I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Patent and Trademark Office all information which is known to me to be material to patentability as defined in 37 CFR section 1.56.

I hereby claim the benefit under 35 U.S.C. section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 U.S.C. section 112, I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 CFR section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this

application: 09/017,519 (Serial No), 02/02/98 , the status of which is

☐ patented, ☒ pending, ☐ abandoned.

application: 08/795,272 (Serial No.), 02/04/97 (Filing Date) , the status of which is

☐ patented, ☒ pending, ☐ abandoned.

POWER OF ATTORNEY: I hereby appoint the following attorney(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

(Name)	(Reg. No.)
Robert M. Padilla	38,987
Carla M. Wong	45,788
John G. Mannix	27,254
Gary Borda	35,455

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Robert M. Padilla

Telephone (set out complete number to be dialed from)

USPTO (650) 604-5104

Further, as a named inventor I certify that the Government of the United States of America, as represented by the Administrator of the National Aeronautics and Space Administration, has ☒ assignment in, or ☐ license to the invention set forth in this application and has the irrevocable right to prosecute this application and to receive the patent.

Wherefore, I pray that Letters Patent be granted to me for this invention or discovery described and claimed in the foregoing specification and claims, and I hereby subscribe my name to the foregoing specification, claims, power of attorney and this petition.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. section 1001; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Full Name of Inventor	Last **Mah**	First **Robert**	Middle or Initial **W.**	
Residence and Citizenship	City **Cupertino**	State or Foreign Country **California**	Country of Citizenship **U.S.A.**	
Post Office	Street No. and Name **10959 Maria Rosa Way**	City and State (or Country) **Cupertino, California**		Zip Code **95014**
Signature			Date	

Full Name of Inventor	Last	First	Middle or Initial	
Residence and Citizenship	City	State or Foreign Country	Country of Citizenship	
Post Office	Street No. and Name	City and State (or Country)		Zip Code
Signature			Date	

Full Name of Inventor	Last	First	Middle or Initial	
Residence and Citizenship	City	State or Foreign Country	Country of Citizenship	
Post Office	Street No. and Name	City and State (or Country)		Zip Code
Signature			Date	

United States Patent & Trademark Office

Office of Initial Patent Examination -- Scanning Division

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